

Supplementary Table 1. Demographic characteristics of women with lupus by treatment status with cyclophosphamide including women who had a hysterectomy before the age of 40

Demographic and clinical characteristics		Ever received Cyclophosphamide				P-value
		Yes N=42	22%	No N=145	78%	
Age at survey	40 - 49	26	62%	80	55%	0.45
	50 - 59	14	33%	44	30%	
	60 - 69	2	5%	19	13%	
	70 - 79	0	0%	2	1%	
Age at diagnosis	20 - 24	10	24%	24	17%	0.16
	25 - 29	8	19%	36	25%	
	30 - 34	15	36%	34	23%	
	35 - 39	9	21%	51	35%	
Race/ ethnicity	Non-Hispanic white	4	10%	28	19%	0.32
	Non-Hispanic black	35	83%	106	73%	
	Other	3	7%	11	8%	
Current marital status	Married	18	43%	62	43%	0.40
	Never married	14	33%	35	24%	
	Other ¹	10	24%	47	33%	
Education	High school or less	6	15%	47	33%	0.02
	More than high school	35	85%	94	67%	
Annual household income	Less than \$20,000	10	26%	48	36%	0.59
	\$20,000 - \$39,999	8	21%	25	19%	
	\$40,000 - \$69,999	10	26%	24	18%	
	\$70,000 or more	11	28%	37	28%	
Insurance	Private	19	50%	65	50%	0.19
	Medicare	14	37%	32	25%	
	Medicaid	5	13%	33	25%	
BILD score	0	5	12%	38	26%	0.06
	1	8	19%	25	17%	
	2-3	12	29%	50	34%	
	≥ 4	17	40%	32	22%	
Secondary amenorrhea before age 40	Yes, not due to a hysterectomy	13	31%	19	13%	0.01
	Yes, due to a hysterectomy	9	21%	31	21%	

No	20	48%	95	66%
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¹Includes separated, divorced, and living with a partner (not married)

Supplementary Table 2. Reproductive health by cyclophosphamide status and self-report of early secondary amenorrhea including women who had a hysterectomy before the age of 40 in the “No early amenorrhea” group

		<u>Ever received Cyclophosphamide</u>					<u>Never received Cyclophosphamide</u>				
		<u>Early secondary amenorrhea</u>		<u>No early amenorrhea¹</u>		<u>P-value</u>	<u>Early secondary amenorrhea</u>		<u>No early amenorrhea¹</u>		<u>P-value</u>
		N=12 ²	33%	N=24	67%		N=17	13%	N=113	87%	
Pregnant ever	Yes	7	64%	23	96%	0.03	15	88%	105	93%	0.62
	No	4	36%	1	4%		2	12%	8	7%	
Pregnancies before lupus	0	6	55%	3	13%	0.02	2	13%	17	16%	1.00
	1	3	27%	7	29%		4	25%	27	26%	
	2 or more	2	18%	14	53%		10	63%	61	58%	
Pregnancies after lupus	0	7	70%	14	70%	1.00	5	29%	12	12%	0.16
	1	2	20%	3	15%		4	24%	26	26%	
	2 or more	1	10%	3	15%		8	47%	63	62%	
Total number of children	0	5	45%	3	14%	0.14	5	29%	12	13%	0.17
	1	4	36%	8	38%		4	16%	21	22%	
	2 or more	2	18%	10	48%		8	47%	62	65%	
Children before lupus	0	6	60%	4	19%	0.09	5	31%	22	23%	0.78
	1	3	30%	9	43%		4	25%	30	30%	
	2 or more	1	10%	8	38%		7	44%	45	46%	
Children after lupus	0	9	82%	18	86%	1.00	13	76%	72	71%	0.92
	1	1	9%	2	10%		2	12%	18	18%	
	2 or more	1	9%	1	5%		2	12%	11	11%	

¹This group includes women who reported no early amenorrhea and those who reported early amenorrhea was experienced due to a hysterectomy.

²A number of women in each group had incomplete pregnancy data so column totals represent the number of women with at least some pregnancy information but may not equal the total number of women in each outcome category

Supplemental Table 3. Comparison of the prevalence of early secondary amenorrhea, ever being pregnant, and ever having a child by cyclophosphamide status and whether the women experienced early menopause including women who had a hysterectomy before the age of 40 in the “No early amenorrhea” group

		Experiencing early secondary amenorrhea		Ever being pregnant		Ever having a child	
		<u>Crude PR (95% CI)</u>	<u>Adj. PR (95% CI)¹</u>	<u>Crude PR (95% CI)</u>	<u>Adj. PR (95% CI)²</u>	<u>Crude PR (95% CI)</u>	<u>Adj. PR (95% CI)²</u>
Ever treated with cyclophosphamide	Yes	2.4 (1.3 - 4.7)	2.6 (1.3 – 5.1)	0.9 (0.8 - 1.1)	0.8 (0.7 - 1.0)	0.9 (0.7 - 1.1)	0.9 (0.7 - 1.0)
	No	ref	ref	ref	ref	ref	ref
Experienced early secondary amenorrhea	Yes	-	-	0.8 (0.6 - 1.0)	0.9 (0.7 - 1.1)	0.7 (0.5 – 0.9)	0.8 (0.6 - 1.1)
	No	-	-	ref	ref	ref	ref

¹A Poisson regression model with a robust variance was used and was adjusted for age at diagnosis, race, education level, income, marital status, current insurance, and BILD score

²A Poisson regression model with a robust variance was used to estimate the effect of treatment with cyclophosphamide and was adjusted for age at diagnosis, race, education level, income, marital status, current insurance, and BILD score. A similar model was used to estimate the effect of early secondary amenorrhea, but was also adjusted for treatment with cyclophosphamide.

Supplementary Table 4. Association between demographic and clinical characteristics and early secondary amenorrhea among women who were not treated with cyclophosphamide including women who had a hysterectomy before the age of 40 in the “No early amenorrhea” group

amenorrhea group		Early secondary amenorrhea		No early amenorrhea ¹		P-value
Demographic characteristics		N=19	13%	N=126	87%	
Age at survey	40 - 49	9	47%	71	56%	0.80
	50 - 59	7	39%	37	29%	
	60 - 69	3	16%	16	13%	
	70 - 79	0	0%	2	2%	
Age at diagnosis	20 - 24	7	37%	17	13%	0.04
	25 - 29	4	21%	32	25%	
	30 - 34	1	5%	33	26%	
	35 - 39	7	37%	44	35%	
Race/ ethnicity	Non-Hispanic white	5	26%	23	18%	0.44
	Non-Hispanic black	12	63%	94	75%	
	Other	2	11%	9	7%	
Current marital status	Married	6	32%	56	45%	<0.01
	Never married	11	58%	24	19%	
	Other ²	2	11%	45	36%	
Education	High school or less	9	53%	38	31%	0.10
	More than high school	8	47%	86	69%	
Annual household income	Less than \$20,000	5	29%	43	37%	0.69
	\$20,000 - \$39,999	5	29%	20	17%	
	\$40,000 - \$69,999	3	18%	21	18%	
	\$70,000 or more	4	24%	33	28%	
Current insurance	Private	8	44%	57	51%	0.43
	Medicare	3	17%	29	26%	
	Medicaid	7	39%	26	23%	
Health and medications						
BILD score	0	6	32%	32	25%	0.38
	1	1	5%	24	19%	
	2-3	6	32%	44	35%	
	≥ 4	6	32%	26	21%	

Kidney transplant	Yes	2	11%	1	1%	0.05
	No	17	89%	125	99%	
Dialysis for > 6 months	Yes	1	5%	4	3%	0.44
	No	18	95%	120	97%	
Hydroxychloroquine	Yes	9	82%	76	81%	1.00
	No	2	18%	18	19%	
Methotrexate	Yes	7	37%	21	18%	0.07
	No	12	63%	99	83%	
Mycophenolate mofetil	Yes	3	16%	9	8%	0.37
	No	16	84%	108	92%	
Steroids	Yes	12	92%	96	90%	1.00
	No	1	8%	11	10%	

¹This group includes women who reported no early amenorrhea and those who reported early amenorrhea was experienced due to a hysterectomy.

¹Includes separated, divorced, and living with a partner (not married)